IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

MICROSPHERIX LLC, Plaintiff, v. MERCK SHARP & DOHME CORP., MERCK SHARP & DOHME B.V. AND ORGANON USA, INC., Defendants.	Civil Action No. 2:17-cv-03984 (CCC/MF) JURY TRIAL DEMANDED

DEFENDANTS MERCK SHARP & DOHME CORP., MERCK SHARP & DOHME B.V. AND ORGANON USA, INC.'S RESPONSIVE CLAIM CONSTRUCTION BRIEF

TABLE OF CONTENTS

Page

TABLE OF AUTHORITIES

Page

Cases

TABLE OF ABBREVIATIONS

Abbreviation	Definition
'193 Patent	U.S. Patent No. 6,514,193 (filed May 18, 2001) (issued February 4, 2003) (D.I. 1-2)
'402 Patent	U.S. Patent No. 9,636,402 (filed May 13, 2015) (issued May 2, 2017) (D.I. 1-1)
'401 Patent	U.S. Patent No. 9,636,401 (filed August 29, 2014) (issued May 2, 2017) (D.I. 1-3)
'835 Patent	U.S. Patent No. 8,821,835 (filed June 13, 2013) (issued September 2, 2014) (D.I. 1-4)
'310 Patent	U.S. Patent No. 7,776,310 (filed September 19, 2003) (issued August 17, 2010)
'128 Provisional	Provisional Appl. No. 60/249,128 (filed November 16, 2000)
'050 Provisional	Provisional Appl. No. 60/412,050 (filed September 19, 2002)
Asserted Patents	the '402, '401, and '835 Patents
IPR	*Inter Partes* Review
POSA	Person of ordinary skill in the art
Park Decl.	Declaration of Dr. Kinam Park, filed concurrently with Merck's Opening Claim Construction Brief (D.I. 103-1)
Ex.	Exhibit to the Declarations of Andrew P. Blythe, filed concurrently with Merck's Opening and Responsive Claim Construction Briefs
Prov.	Provisional
Fig.	Figure
Grimm	U.S. Patent No. 5,938,583 (filed December 29, 1997) to Grimm (issued August 17, 1999)
Taber	Taber's Cyclopedic Medical Dictionary, 19th edition (2001)
Stedman	Stedman's Medical Dictionary, 27th Edition (2000)
Merriam	Merriam-Webster's Medical Desk Dictionary, Revised Edition (2002)
Webster	Webster's II New College Dictionary (1999)
Dorland	Dorland's Illustrated Medical Dictionary, 30th Edition (2003)

Abbreviation	Definition
Mosby	Mosby's Medical Dictionary, 6th Edition (2002)
Fraser	"New prospects for luteinizing hormone releasing hormone as a contraceptive and therapeutic agent" by H M Fraser, dated October 9, 1982
'402 FWD	Final Written Decision, IPR2018-00393 (Paper 43), dated July 8, 2019
'401 FWD	Final Written Decision, IPR2018-00402 (Paper 44), dated July 8, 2019
'835 FWD	Final Written Decision, IPR2018-00602 (Paper 43), dated July 8, 2019
PTO	United States Patent and Trademark Office
PTAB	Patent and Trial Appeal Board
MX Ev.	Microspherix's Rebuttal Claim Construction Evidence (served September 1, 2020)
1/12/12 Pros. Tr.	Oral argument transcript for the January 12, 2012 hearing before the PTAB from the prosecution file of U.S. Patent Appl. No. 10/852,407
MX Inf. Cont.	Microspherix's Preliminary Disclosure of Asserted Claims and Infringement Contentions Against Defendants (served March 7, 2018)
MX Val. Cont.	Microspherix's Preliminary Responsive Validity Contentions (served June 8, 2018)
SDG Rep.	SDG Report No. 4678, dated October 1996
'401 POR	Patent Owner's Response, IPR2018-00402, Paper 24, dated October 23, 2018
'401 POPR	Patent Owner's Preliminary Response, IPR2018-00402, Paper 8, dated May 7, 2018
'401 FH Srch.	Examiner's Search Strategy and Results, dated April 18, 2016, from the prosecution file of U.S. Patent Appl. No. 14/473,159, which issued as U.S. Patent No. 9,636,401
Kiser Decl.	Declaration of Dr. Patrick F. Kiser, Ph.D. in IPR2018-00402 (Ex. 2001), dated May 7, 2018
'402 POPR	Patent Owner's Preliminary Response, IPR2018-00393 (Paper 6), dated April 10, 2018

Abbreviation	Definition
'402 POR	Patent Owner's Response, IPR2018-00393 (Paper 24), dated October 23, 2018
'402 POSR	Patent Owner's Sur-Reply, IPR2018-00393 (Paper 34), dated March 5, 2019
IPR Hr'g Tr.	Transcript from April 8, 2019 Oral Hearing for IPR2018-00393 ('402 Patent), IPR2018-00402 ('401 Patent), IPR2018-00602 ('835 Patent) (Paper 42 in IPR2018-00393)
MX Hr'g Sl.	Microspherix's Demonstratives for April 8, 2019 Oral Hearing for IPR2018-00393 ('402 Patent), IPR2018-00402 ('401 Patent), IPR2018-00602 ('835 Patent) (Ex. 2153 in IPR2018-00393)
MX Op. Br.	Microspherix's Opening Claim Construction Brief (D.I. 107)
MX Ex.	Exhibit to Microspherix's Opening Claim Construction Brief (D.I. 107-1)
Park Tr.	Transcript from December 10, 2020 deposition of Dr. Kinam Park
Park Dep. Ex.	Exhibit from December 10, 2020 deposition of Dr. Kinam Park
MRK Op. Br.	Merck's Opening Claim Construction Brief (D.I. 103)
Col.	Column
Cl.	Claim
Oxford	Oxford Concise Medical Dictionary, New Edition (2000)
Brem	U.S. Patent No. 5,626,862 (filed August 2, 1994) to Brem (issued May 6, 1997) (Ex. 1004 in IPR2018-00393)
'402 Pet.	Petition for *Inter Partes* Review, IPR2018-00393 (Paper 1), dated December 22, 2017
'402 Pre. Amd.	Preliminary amendment, dated May 13, 2015, from the prosecution file of U.S. Patent Appl. No. 14/473,159, which issued as U.S. Patent No. 9,636,402
'402 PER	Petitioner's Reply, IPR2018-00393 (Paper 27), dated January 23, 2019

TABLE OF PARTIES' PROPOSED CONSTRUCTIONS

Claim Term	Merck's Proposal	Microspherix's Proposal
"**target tissue**" '401 Patent claims 1–5, 9, 10, 13–16, 18–19, and 25 '835 Patent claims 1, 3, 4, 10, 16, and 20	"the tissue into which the implantation is intended and on which the agent acts to produce its intended effect"	Plain and ordinary meaning, "tissue into which implant is implanted"
"**seed, for implantation into a subject**" '835 Patent claims 1, 3, 4, 10, and 16	"seed, for implantation into a subject at or near the site on which the agent acts to produce its intended effect"	Plain and ordinary meaning, "implant shaped to pass through a needle bore, for implantation into a subject"
"**strand for administration of a therapeutic agent to a subject in need thereof**" '402 Patent claims 6, 9	"strand for administration of a therapeutic agent that acts to produce its intended effect at or near the implantation site in a subject in need thereof"	Plain and ordinary meaning, "elongated implant for administration of a therapeutic agent to a subject in need thereof"
"**strand for implantation into a subject**" '401 Patent claims 1–5, 9, 10, 13–16, and 18–19	"strand for implantation into a subject at or near the site on which the agent acts to produce its intended effect"	Plain and ordinary meaning, "elongated implant for implantation into a subject"
"**therapeutic agent**" '402 Patent claims 6, 9 '401 Patent claims 1–5, 9, 10, 13–16, 18–21, 23–25 '835 Patent claims 1, 3, 4, 10, 16, 17, and 20	"an agent for the treatment of disease"	Plain and ordinary meaning, "agent that exerts a desired medically beneficial or physiological effect"

Claim Term	Merck's Proposal	Microspherix's Proposal
"**prophylactic agent**" '401 Patent claims 1–5, 9, 10, 13–16, 18–21, and 23–25 '835 Patent claims 1, 3, 4, 10, 16, 17, and 20	"an agent for the prevention of disease"	Plain and ordinary meaning, "agent for prevention of an undesired or non-beneficial physiological condition"
"**marker component**" '401 Patent claims 1–5, 9, 10, 13–16, 18–21, and 23–25 '835 Patent claims 1, 3, 4, 10, 16, 17, and 20	"the part of the seed/strand that is a marker"	Plain and ordinary meaning, "component of a device that comprises a marker"
"**hollow interior**" '401 Patent claims 1–5, 9, 10, 13–16, 18–21, and 23–25 '835 Patent claims 1, 3, 4, 10, 16, 17, and 20	"an empty space defined by and inside the wall of the marker component"	Plain and ordinary meaning, "interior space"
"**wherein the agent is disposed within the hollow interior of the tube**" '835 Patent claim 20	"wherein the agent is disposed within the empty space defined by and inside the wall of the marker component"	Plain and ordinary meaning, "where in the agent is disposed within the interior space of the tube"
"**[marker component] . . . having a substantially continuous wall bounding a hollow interior**" '401 Patent claims 1–5, 9, 10, 13–16, and 18–19 '835 Patent claims 1, 3, 4, 10, 16, and 20	The marker component itself constitutes a wall that defines the hollow interior.	Plain and ordinary meaning, "[component of a device that comprises a marker] . . . having a substantially continuous wall bounding a hollow interior"

Claim Term	Merck's Proposal	Microspherix's Proposal
"**[marker component] . . . having a substantially continuous wall along the length, the substantially continuous wall bounding a hollow interior**" '401 Patent claims 20– 21, and 23–25 '835 Patent claim 17	The marker component itself constitutes a wall that defines the hollow interior.	Plain and ordinary meaning, "[component of a device that comprises a marker] . . . having a substantially continuous wall along the length, the substantially continuous wall bounding a hollow interior"
"**polymeric coating**" '402 Patent claims 6, 9	"a layer of polymer that is formed as a result of applying it or building it up to cover the existing surface of the strand/implantable rod"[1]	Plain and ordinary meaning, "a layer of polymer"
"**rod**" '402 Patent claims 6, 9	"a unitary cylinder"	Plain and ordinary meaning, "cylinder-shaped device"
"**flexible**" '401 Patent claims 1–5, 9, 10, 13–16, 18–21, and 23–25	Indefinite Alternatively: "capable of bending"	Not indefinite, plain and ordinary meaning, "not rigid or flaccid"
"**marker**" '401 Patent claims 1–5, 9, 10, 13–16, 18–21, and 23–25	"a substance less toxic than barium sulfate that is added to enhance imageability"	Plain and ordinary meaning, "material included for detection using standard imaging techniques"

[1] Replacing the phrase "to cover" in Merck's construction with "on" would not change the substance of the construction if the Court finds it is a more appropriate construction.

Claim Term	Merck's Proposal	Microspherix's Proposal
'835 Patent claims 1, 3, 4, 10, 16, 17, and 20		
"**radio-opaque material**" '402 Patent claims 6, 9	"a substance less toxic than barium sulfate that can be detected by conventional x-ray imaging techniques"	"material that can be visualized by conventional x-ray imaging"
"**agent . . . selected from the group consisting of . . . radiopaque**" '401 Patent claim 15 '835 Patent claim 16	"a substance less toxic than barium sulfate that can be detected by conventional x-ray imaging techniques"	"agent . . . selected from the group consisting of . . . material that can be visualized by conventional x-ray imaging"
"**radio-opaque**" and "**radiopaque**" '402 Patent claims 6, 9 '401 Patent claim 15 '835 Patent claim 16	"detectable by conventional x-ray imaging techniques"	"capable of visualization by conventional x-ray imaging"

I. INTRODUCTION

Microspherix asserts three patents, all of which are entitled "Brachytherapy," and all of which describe the claimed invention as existing within the field of "brachytherapy," which the patents themselves explain is the *localized* treatment of *disease*. Each also states, in the very first substantive line of the specification: "This application relates to imagable implantable brachytherapy devices, and methods of use thereof." '402 Patent at 1:28-29. Yet to achieve the claim constructions it needs to allege infringement of Merck's contraceptive product—which does not treat any disease and does not administer any agent in a localized manner—Microspherix eviscerates all meaning from the patents' expressly stated basis in brachytherapy.

The patents set forth clearly and plainly the three elements of brachytherapy: (1) localized, (2) treatment of disease, with (3) radioactive agents. *Id.* at 1:28-41. The patents contemplate using non-radioactive drugs in addition to or in place of radioactive agents, but they never discuss deviating from the *localized* treatment of *disease*. If they did, there would be no point in describing the invention as brachytherapy, as it would lack all three stated aspects of brachytherapy. Instead, the patents' *Summary of the Invention* makes clear that the advantage of the claimed invention relates to the benefits of localized treatment over the treatment of remote diseased tissue. "Since concentrations of the therapeutically active substance will be greater at the implantation site (*e.g.*, the diseased tissue), any potential deleterious

effect of the therapeutically active substance on healthy tissue located away from the implantation site will be reduced." *Id.* at 4:21-25.

The intrinsic record provides no support for Microspherix's expansion of the claim scope, so Microspherix suggests that the inventor left oblique clues in the specification (three in total—namely isolated and incorrect interpretations of the single words "may" and "e.g.," and an *implied*, anti-contextual characterization of classes of drugs), which clues, when deciphered, ultimately reveal to the POSA that the inventor, *without coming out and saying it*, actually entirely redefined the word "brachytherapy" to cover non-localized delivery of any agent, whether for the treatment of disease or otherwise. Said another way, Microspherix would have the Court believe that the patentee subtly, via disconnected clues, actually redefined "brachytherapy" to have zero relation to brachytherapy.

But Microspherix cannot explain why a POSA would think to solve this hidden puzzle to arrive at such an unlikely conclusion, rather than accept what the patents plainly state on their face: that the invention is directed to localized treatment of disease, for precisely the advantages and benefits that the patents expressly describe. Contrary to Microspherix's suggestion, a POSA would not simply ignore what is plainly stated in the patents in favor of Microspherix's contextless and logically flawed interpretations. This conclusion is reinforced by the fact that Microspherix waited more than fourteen years after the original priority application

was filed, and until it had Merck's Nexplanon product in mind, to interpret its patents as encompassing anything other than implants for the localized treatment of disease. Contemporaneous disclosure speaks louder than litigation-driven words. Microspherix now seeks precisely the type of *post hoc* expansion of the patent scope that the claim construction process is intended to guard against.

For many of the claim terms, Microspherix focuses entirely on attacking Merck's constructions, rather than providing any justification or support for its own constructions. Microspherix asserts *ipse dixit* that its constructions are "plain and ordinary," but such assertions are nothing more than unsupported attorney argument, and therefore carry no weight. As Microspherix concedes, "[d]etermining the meaning of claim terms requires reading the words used in the patent documents *with an understanding of their meaning in the field*" and the terms "must be understood and interpreted by the court *as they would be understood and interpreted by a person in that field of technology*." MX Op. Br. at 4-5 (quoting *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005)) (citations omitted).[2] Applying this black letter law, Merck's constructions, which are compelled by the intrinsic record and confirmed by the unrebutted testimony of Merck's expert, Dr. Park—reflect the plain and ordinary meaning. The Court should adopt Merck's constructions.

II. TERMS RELATING TO LOCALIZED TREATMENT OF DISEASE

[2] All emphases added unless otherwise noted.

A. "target tissue"

As set forth in its opening brief, Merck's construction follows from the intrinsic record as understood by a POSA and is consistent with the common meaning of the term in the field of the alleged invention. The specification consistently uses the term "target tissue" to refer to the tissue *targeted by the implant's agent* (*i.e.*, the tissue on which the agent acts to produce its intended effect). MRK Op. Br. at 10-11. The entire intrinsic record focuses on the "delivery" of the agent to, the "concentrations" of agent within, the "dosing of," and the "*treat[ment]*" of the "target tissue." *Id.* (citing '402 Patent at 5:28-33, 15:42-49, 16:15-24, 17:42-46, 18:21-25, 23:41-44; '128 Prov. (Ex. 3) at 29; Park Decl. ¶ 75). A POSA would thus understand that the tissue is the "target" of the agent, not simply the location of the implant. *Id.* at 12. The specification reflects this. While distinguishing prior art "systemic administration" such as "oral or intravenous delivery" as inferior, the specification describes the remote tissue targeted by systemically administered agents as the "target tissue," even though the referenced systemic prior art involves no implants. *Id.* at 12, 17. This indicates that "target tissue" must refer to the tissue that is the *target of treatment*. This is consistent with a POSA's understanding and use of the term "target tissue" as the tissue targeted for the agent's effect.[3] *Id.* at 14; Park Decl. ¶ 81.

[3] During deposition, Microspherix questioned Dr. Park regarding an excerpt

In the context of the localized *brachytherapy* implants described in the Asserted Patents, "target tissue" refers to both its common and ordinary meaning described above (the target of the treatment) *and* the tissue where implantation occurs. Notably, the patent uses a *different term* ("implantation site") to indicate *just* the location of the implant without regard to the location of treatment. MRK Op. Br. at 12. In other words, the patent uses "implantation site"—*not* "target tissue"—when referring to what is described by Microspherix's construction. By ignoring the primary meaning of the term "target tissue" (the target of the intended treatment), Microspherix's construction furthermore is indistinct from the term "tissue" alone and thus fails to give meaning to the term "target," since an implant is by definition implanted into tissue at the location of implantation. *Id.* at 9-10.

In its opening brief, Microspherix fails to provide a single citation, argument, or justification for its own construction, simply asserting via unsupported attorney argument that its proposal reflects a "plain and ordinary meaning." MX Op. Br. at 17. The Court should reject this *ipse dixit* and Microspherix's construction with it,

---

regarding transdermal drug delivery in a 2017 textbook that Dr. Park edited but did not author. The excerpt describes the internal dermal layer of the skin as the "'target tissue'" in a "transdermal delivery approach" in which a drug is administered to the external epidermis layer. Park Dep. Ex. 6 (Ex. 33) at 219. Although the authors appear to use "target tissue" to describe where the drug *reaches* rather than what the drug *affects*, the focus is on the action of the drug. The authors depart from the normal meaning of "target tissue" as indicated by the use of quotation marks around the term. Regardless, it is telling that Microspherix's sole example of "target tissue" post-dates the prior art by sixteen years and is inconsistent with its own construction.

and should not allow Microspherix to come forth for the first time in response with support for its construction; Microspherix has waived such arguments.[4] By grouping "target tissue" with the disputed preamble terms, Microspherix ignored the significant textual basis in the intrinsic record for Merck's construction: Microspherix failed to address a single one of the thirty times the term "target tissue" appears in the specification. Rather, Microspherix rests its entire argument on a single dependent claim from a related patent—claim 2 of the '193 Patent, and unsupported conjecture about the "typical" nature of therapeutic agents. *Id.* at 15. This reliance neither helps Microspherix nor contradicts Merck's construction.

The '193 patent claims "[a] method for administering a **therapeutically active component** to a **target tissue** in a subject." '193 Patent, Cl. 1. Dependent claim 2 further requires that "the target tissue" to which the therapeutically active component is administered "is a diseased tissue." *Id.*, Cl. 2. Microspherix thus argues that target tissue must be broader than diseased tissue, and that therefore Merck's construction is incorrect. As Microspherix itself notes, however, the term "therapeutically active component" includes both agents that treat diseased tissue

[4] To the extent that Microspherix had arguments to make in support of any of its own constructions, it needed to make those in its opening brief. Having failed to do so for numerous constructions, Microspherix has waived any such arguments. *Bayer AG v. Schein Pharm., Inc.*, 129 F. Supp. 2d 705, 716-17 (D.N.J. 2001), *aff'd*, 301 F.3d 1306 (Fed. Cir. 2002). If Microspherix raises new arguments or evidence in its response, Merck reserves the right to move to strike or seek supplemental briefing.

and agents that are "prophylactic." MX Op. Br. at 12. Because prophylactic agents *prevent* disease, or in Microspherix's proposal, prevent "an undesired or non-beneficial physiological condition," the "target tissue" in prophylactic applications of the claimed implants *may not yet be* "diseased." The fact that "target tissue" is broader than and not limited only to "diseased tissue" is therefore entirely consistent with Merck's construction. Claim 2 of the '193 Patent simply specifies that the "therapeutically active component" in that claim is *treating* disease, as opposed to *preventing* tissue from becoming diseased. Either way, the target tissue is still the tissue upon which *the agent acts to produce its intended effect*, as reflected in Merck's construction. This is consistent with Dr. Park's deposition testimony that a POSA reading the claims of the '193 Patent would understand that "sometime[s] the target tissue may not be diseased yet. For example, when you deliver prophylactic agent." Park Tr. (Ex. 34) at 69:2-4.

A further reason that "target tissue" being broader than the "diseased tissue" is consistent with Merck's construction is that even with therapeutic agents that *treat* disease, a POSA may intentionally target nearby healthy tissue in order to ensure complete efficacy. *See* Brem (Ex. 35) at 3:51-63 (prior art cited on the face of the patent describing implantation of chemotherapeutic implants either "within or immediately adjacent the tumors to be treated or the site where they have been surgically removed"); Park Tr. (Ex. 34) at 69:5-9 ("[W]hen you implant hundreds of

a seed or strand, not all of them probably go to diseased tissue. Some of them be slight[ly] outside, for a lot of reasons."). This was common in the field of cancer treatment in which the invention is grounded, where tumor boundaries are difficult to define and where cancer cells must be completely eradicated during therapy to prevent later remission. *E.g.*, Brem (Ex. 35) at 1:21-30 (describing recurrence of malignancies within the tissue adjacent to a resected tumor). Merck's construction is thus consistent with the cited claims of the '193 patent.

Microspherix also argues that Merck's construction of "target tissue" is flawed because it creates tension between claims 1 and 15 of the '401 patent. No such tension exists. Microspherix points out that Merck's construction of "target tissue" precludes the use of *some* of the "typical[]" agents that might otherwise fall within the classes enumerated in dependent claim 15 of the '401 Patent. MX Op. Br. at 15-16. But claim 15 is entirely consistent with Merck's construction. Even if Microspherix is correct about the scope of potential "agents" in the invention (it is not, *infra* at 16-19), it is routine that the inventor's decision to add one claim limitation (*i.e.*, "target tissue" in claim 1) may also limit the feasible embodiments of another (*e.g.*, "agent" in claim 15). Microspherix's argument is thus incorrect.

Finally, Microspherix's assertion (MX Op. Br. at 15) that Merck's construction of "target tissue" transforms the claims from "apparatus claims" to "method of treatment claims" is simply incorrect. Merck's construction of "target

tissue" merely identifies *which* "tissue" is the "target"—*i.e.*, the one both in which implantation is intended and on which the agent acts to produce its intended effect. Merck's construction ("tissue into which implantation is intended . . .") does not require "actual placement of a strand in the target tissue" any more than Microspherix's construction does ("tissue into which implant is implanted"). Nor does Merck's construction require that the agent actually "act." Microspherix failed to set forth evidence or argument either supporting its own construction or effectively contradicting Merck's. The Court should adopt Merck's construction.

B. "seed, for implantation into a subject" / "strand for administration of a therapeutic agent to a subject in need thereof" / "strand for implantation into a subject"

Since the earliest provisional filings over twenty years ago, the intrinsic records of the Asserted Patents have consistently characterized the alleged invention as "brachytherapy," which the patents themselves describe as "[r]adioactive seed therapy" "for treating various medical conditions, most notably prostate cancer" in which dozens if not hundreds of "small seeds containing a radioisotope that emits a relatively short-acting type of radiation are surgically implanted *in the diseased tissue*." '402 Patent at 1:28-41. The patents explain that brachytherapy is "advantageous" "***[b]ecause*** the seeds are *localized near the diseased tissue*," and thus "the radiation they emit is thereby concentrated on the cancerous cells and *not on distantly located healthy tissue*." *Id.* The patents themselves expressly set forth

the three elements of brachytherapy: the (1) localized treatment (2) of diseased tissue (*i.e.*, cancer[5]) (3) with a radioisotope.[6] *Id.* While the patents indicate that a non-radioactive drug can be used "as an alternative to[] a radioisotope" (*id.* at 4:1-3), not a single disclosure tells a POSA that the "brachytherapy" implants of the Asserted Patents extend beyond the (1) *localized* administration of agents to (2) treat disease. Microspherix's proposal to divorce "brachytherapy" from both (1) localized administration, which is the very meaning of the root "brachy," and (2) treatment of disease would render this titular adjective of the invention utterly meaningless.

The Summary of the Invention ("Summary") attributes the same localization advantage of prior art brachytherapy to the purported invention as a whole:

> Since concentrations of the therapeutically active substance will be ***greater at the implantation site (e.g., the diseased tissue)***, any potential deleterious effect of the therapeutically active substance on ***healthy tissue located away from the implantation site*** will be reduced.

Id. at 4:21-25. This advantage is not attributed to merely one of "various possible

---

[5] As noted in Merck's opening brief, the Court need not reach the issue of whether the patent is limited to the treatment of ***cancer*** to accept Merck's positions.

[6] Numerous contemporaneous medical dictionaries comport with the patent's description of "brachytherapy," including the disclosed advantage of localized treatment. *See* Mosby (Ex. 10) at 233 ("brachytherapy: [Gk, *brachys*, short, *therapeia*, treatment], the placement of radioactive sources ***in contact with or implanted into the tumor tissues to be treated*** for a specific period. The rationale for this treatment is to provide a high absorbed dose of radiation ***in the tumor tissues and a very limited absorbed low dose in the surrounding normal tissues***."); *see also* Taber's (Ex. 1) at 282 ("***at the treatment site***"); Oxford (Ex. 36) at 83 ("***into or close to a tumour***"); Merriam (Ex. 9) at 99 ("***in or close to the area being treated***").

embodiments" as Microspherix suggests when presenting only snippets of this language in its opening brief (MX Op. Br. at 4), but to "the strands" of the invention described in the Summary without reservation. The Summary furthermore states without caveat that the therapeutically active substances "*will be*" concentrated at the implantation site and harmful effects on remote healthy tissue "*will be reduced*," and otherwise distinguishes systemic administration as inferior. '402 Patent at 4:21-25, 5:29-33; s*ee C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 864 (Fed. Cir. 2004) ("Statements that describe the invention as a whole are more likely to be found in certain sections of the specification, such as the Summary of the Invention."). There is not a single disclosure or embodiment in the specification indicating that the implants are to be used, much less can be used, to administer therapeutically active substances to remote tissues. Rather, the patent describes implants with features specifically designed to assist with localized treatment: anchoring structures to preserve local patterns of administration, markers to assist with precise placement within target tissue, and geometries designed for use with existing brachytherapy devices and techniques. MRK Op. Br. at 18-19.[7]

[7] While method claims of the formerly asserted '193 Patent include the term "brachytherapy" (*i.e.*, "brachytherapy seed") and the Asserted Claims do not, claim differentiation would not support reading the Asserted Claims to be intended for applications broader than described in the patents. Indeed, Microspherix argued in opposition to Merck's motion to dismiss (D.I. 35 at 17) that the term "brachytherapy" itself, in the context of the claims of the '193 Patent, describes the characteristics of the "seed" rather than the manner of its use and is "simply the

The law is clear that where an inventor has so limited the scope of the invention, the claims should be construed accordingly. *SciMed Life Sys. Inc. v. Adv. Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1341 (Fed. Cir. 2001); *Toro Co. v. White Consol. Indus., Inc.*, 199 F.3d 1295, 1301 (Fed. Cir. 1999). Microspherix's citation of *Liebel–Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898 (Fed. Cir. 2004) is easily distinguished. There, the Federal Circuit reversed a limiting claim construction that the district court had based solely on the *absence* of alternative embodiments. *Id.* at 906-07. Here, the inventor has expressly and uniformly described his invention as "brachytherapy," a technique that at bottom requires localized administration, and attributed to his invention advantages that are absent from the systemic administration he *criticizes* and distinguishes as inferior.

Microspherix argues that despite the language in the Summary describing the localized administration as superior to systemic administration and the consistent description of the invention as "brachytherapy," the inventor left three subtle hints that *imply* the invention extends to systemic administration. There is not a single

---

name[] for objects used in the claimed method." Thus, Microspherix confirmed that the difference, if any, between a "brachytherapy seed" and a "seed" in the '193 Patent is *irrelevant* to whether the preambles of the Asserted Patents, ***which include language beyond just "seed" or "brachytherapy seed,"*** impact the manner of use. Here, the intended use of the claimed seeds and strands in the Asserted Patents manifests in the preamble language: "*for implantation*" ('401 and '835 Patents) and "*for administration of a therapeutic agent*" ('402 Patent), indicating, in the context of the Asserted Patents, treatment or prevention of disease local to the implant.

statement in the specification supporting Microspherix's argument that the scope of the invention extends to systemic administration. Microspherix's position instead hangs on context-free inferences drawn from single instances of the words "*e.g.*" and "may," and a logically flawed argument based on a listing of classes of agents that includes examples, such as "hormones," that, according to Microspherix, are "typically" used for systemic treatment. All of Microspherix's arguments misinterpret the specification and fail to support its construction.

First, Microspherix's reliance on the specification's single use of the term "e.g." again misconstrues the relationship between the implants of the invention and "diseased tissue," as described above (*supra* at 6-8). When stating that localized delivery is an advantage of the invention, the patent parenthetically lists "diseased tissue" as an example "implantation site." '402 Patent at 4:21-23 ("Since concentrations of the therapeutically active substance will be greater at the **implantation site (e.g. the diseased tissue**), any potential deleterious effect of the therapeutically active substance on healthy tissue located away from the implantation site will be reduced."). As explained above, "diseased tissue" is only an example of the "implantation site" because, *as the parties agree*, the implants of the invention may contain a "prophylactic" agent and thus may be implanted in tissue that the agent targets but that is *not yet* diseased. In either event, *the tissue is that upon which the agent is intended to act*. A POSA furthermore would recognize that

the "implantation site" could be immediately adjacent to the "diseased tissue" to ensure complete eradication of disease, such as prior art cancer-treatment methods. *See* Brem (Ex. 35). This does not change the localized nature of the treatment.

Merck does not equate "diseased tissue" with the tissue on which the agent acts. By attributing this strawman position to Merck, Microspherix incorrectly reasons that therefore, if "diseased tissue" is only an example ("e.g.") of the "implantation site," then *by implication* the implant can be implanted outside of and even *remotely* to the tissue on which the agent acts. MX Op. Br. at 16 ("'diseased tissue' . . . is not (as Merck would require) the ***only*** type of 'target tissue'") (emphasis in original). But as described above, there are several reasons that the "target tissue" in the localized delivery of the invention may not be a "diseased tissue," and thus the location of the "implantation site" in tissues that are not diseased is entirely consistent with Merck's construction. In fact, the very sentence containing the "e.g." parenthetical at issue is describing the advantage of placing the implant ***locally*** to the site where the therapeutically active substance should be concentrated to have its intended effect. Microspherix's reasoning is logically flawed *and* anti-contextual.

The next clue, according to Microspherix, is the use of "may" in a transition statement in the specification to suggest that the patents extend to undescribed embodiments. MX Op. Br. at 16. In Section I.C. describing the "Therapeutic and Diagnostic Agents" for inclusion in the "Brachytherapy Strands," one paragraph

begins by stating that "[t]he claimed brachytherapy seed or strand ***may*** also be used for local cancer therapy." '402 Patent at 10:1-2. This paragraph follows several paragraphs describing embodiments that are also used exclusively "for local cancer therapy." *Id.* at 10:1-5. Thus, the sentence in question is not, as Microspherix suggests, drawing a contrast to a description of something differing from local cancer therapy. As further described below (*infra* at 16-18), the section first identifies specific "anti-neoplastic" and "radiosensitizing agents" as examples of "non-radioactive drugs." *Id.* at 8:4-15. Both are for the treatment of cancer, and radiosensitizing agents, which sensitize tissue to radiation in conjunction with a radioactive component, are exclusively "for local cancer therapy." Park Decl. ¶ 41. After describing prior art examples of the use of biocompatible materials ('402 Patent at 8:16-9:30), the three paragraphs immediately preceding the transition sentence in question describe embodiments of "thermoseeds," which apply "heat to a target tissue for the purpose of killing cancerous cells." *Id.* at 9:31-67. Such thermoseeds are exclusively "for local cancer therapy." Thus, the statement that the claimed implants "*may* also be used for local cancer therapy" simply sets up that paragraph and does not represent a transition away from implants that are *not* "for local cancer therapy."

Not only is Microspherix's reading contradicted by the discussion of other local cancer therapies immediately prior to the excerpt Microspherix relies upon,

but, critically, the patent lacks any actual description of such allegedly non-local examples. The Federal Circuit has previously rejected Microspherix's inferential approach to expanding the scope of claims. In *Wang Labs., Inc. v. Am. Online, Inc.*, 197 F.3d 1377 (Fed. Cir. 1999), the patentee argued that the claims were not limited to the only disclosed embodiment in the specification because it was prefaced as a merely "***preferred*** embodiment." *Id.* at 1383. The Federal Circuit rejected this argument, noting that "[w]hether an invention is fairly claimed more broadly than the 'preferred embodiment' in the specification is a question specific to the content of the specification" and that "[t]he usage 'preferred' does not of itself broaden the claims beyond their support in the specification." *Id.* Here, the specification's use of "may also" is of no moment to whether the invention is limited to "local cancer therapy" where there is no disclosure of any other type of therapy in the patent, and the specification in fact expressly describes the invention as localized brachytherapy.

Microspherix's final argument, that the listed classes of potential agents at col. 8:4-15 (of the '402 patent) includes ones, such as "hormones," that are "typically . . . used for systemic effect," (MX Op. Br. at 15) is not only unsupported attorney argument with respect to what is "typical" (and therefore merits no weight) but also is entirely at odds with the context in which the listing occurs. Simply looking beyond the snippet that Microspherix excerpts negates Microspherix's argument entirely. The portion of the specification relied upon by Microspherix appears in a

subsection of the specification under the main heading "***Brachytherapy*** Strands." Under this heading of "Brachytherapy," the patent explains that "[a]ny of a wide range of therapeutic, diagnostic and prophylactic materials can be incorporated into the strands," and in particular the "non-radioactive drug can take the form of" one of several classes of drugs such as "antibiotics," "cytotoxic . . . agents," or "hormones" among others. '402 Patent at 7:65-8:10. While brachytherapy strands of the invention may include a drug for localized delivery that falls within a broader class of, *e.g.*, "hormones" or "antibiotics," it does not follow—and the patent does not indicate—that therefore ***all*** hormones or ***all*** antibiotics fall within the scope of the invention, or that any such drugs should be delivered systemically in violation of the express nature and advantage of the invention. That is a leap invented entirely by Microspherix.

Microspherix's reading of this language assumes without basis that the invention encompasses all "hormones" or other agents, including those that are intended for systemic use—*i.e.*, outside of the overlap with the "brachytherapy" section of the specification in which this paragraph appears.[8] But the patents in suit

[8] As noted in Merck's opening brief, the specification describes the list of articles beginning at 8:16 of the '402 Patent as examples of the association of agents with polymers in the prior art, not as exemplary agents for use in the invention. MRK Op. Br. at 13 n.7. For example, as Dr. Park has testified, the "Rosa" article cited in association with "hormones" ('402 Patent at 9:19-20) describes the use of insulin for testing stability in polymer microspheres, but not for administration. Park Decl. ¶ 42; Park Tr. (Ex. 34) at 169:12-171:4. Indeed, insulin could not be safely released

do not say this—not anywhere. Nothing in this section of the patent purports to expand or redefine the context of the invention, which is expressly stated as brachytherapy. Microspherix's entirely unsupported attorney assertion that the agents falling within these classes are "typically" employed systemically has no bearing on the scope of the invention and, in fact, implicitly admits that there are agents falling in the described classes that not only *can be* but *have been* administered locally. In fact, the remainder of the paragraph in question provides specific examples of such a "non-radioactive drug," all of which are "anti-neoplastic" or "radiosensitizing" agents, both of which are consistent with, if not limited to, the ***local*** treatment of cancer. Park Decl. ¶ 41. A POSA would not read backwards from the word "hormones" an implication that, because ***some*** hormones are "typically" administered systemically, the inventor intended not only to alter the scope of the invention but also to redefine the term "brachytherapy" entirely. Park Tr. (Ex. 34) at 134:13-135:6. Even if the patent were to list agents that have not yet been employed locally in the prior art, the patent is still instructing a POSA that such agents could be administered locally with the brachytherapy implants described in the patent to obtain the advantage of the alleged invention. *See* Park Tr. (Ex. 34) at 86:1-21; 173:10-16 (distinguishing between drugs that have system-wide effect and

---

from the implants of the invention as it must be administered at precise times to control glucose levels. *See* Park Tr. (Ex. 34) at 170:14-21.

drugs that travel through systemic circulation to reach their target).

Microspherix again incorrectly claims that Merck's constructions add "method" limitations to an "apparatus" claim. Merck's constructions only clarify where the implantation occurs (*e.g.*, "seed, for implantation into a subject **at or near** the site on which the agent acts to produce its intended effect") or where the administered agent is intended to act (*e.g.*, "strand for administration of a therapeutic agent that acts to produce its intended effect **at or near** the implantation site in a subject in need thereof"). The preambles already require the seed or strand be "for implantation" or "for administration," so Merck's constructions are not adding any limitations of a different nature from the claim language itself.

C. "therapeutic agent" / "prophylactic agent"

The patent provides no special definition of "therapeutic agent" or "prophylactic agent" and thus employs their customary meanings as agents for the treatment and prevention of disease. It is unsurprising that the patent does not define these terms: they have well defined and broadly accepted meanings in the field of the invention that are consistent with the patent's focus on "brachytherapy." MRK Op. Br. at 21-23; Park Decl. ¶ 83. Although Microspherix repeatedly refers to its constructions as "plain meaning usages," it provides no basis or explanation, relying on bare attorney argument. The meaning of the terms *to a POSA*, which Dr. Park provides, is the only "plain meaning" that is in the record. *See Phillips*, 415 F.3d at

1313 ("That starting point is based on the well-settled understanding that inventors are typically persons skilled in the field of the invention and that patents are addressed to and intended to be read *by others of skill in the pertinent art*."). Dr. Park's understanding is reinforced by contemporaneous medical dictionaries. *See* Stedman (Ex. 8) at 1458, 1821; Taber (Ex. 1) at 1763, 2170; Merriam (Ex. 9) at 670, 824; Mosby (Ex. 10) at 1413.

To oppose Merck's construction, Microspherix cobbles together its constructions from two snippets of non-definitional language in the specification but provides no rationale for doing so. First, Microspherix incorrectly asserts that the patent "equates the concept of a 'therapeutic' to something that exerts 'a desired medically beneficial effect.'" MX Op. Br. at 11 (citing '402 Patent at 14:51-56). Although the patent has a section I.C. titled "Therapeutic and Diagnostic Agents" in which it describes the agents to be included in the claimed invention, Microspherix quotes from a passage in a different section: Section IV. titled "Method of Making Brachytherapy Strand for Implantation" that discusses the appropriate size and shape of the strands. The passage-at-issue states:

> In addition, in some applications, the strand should also be large enough to carry ***a sufficient amount*** of the therapeutically active component to be therapeutically active (i.e., a therapeutically effective ***amount*** or ***an amount*** that exerts a desired medically beneficial effect).

'402 Patent at 14:51-56. Far from defining "therapeutic agent" or "prophylactic agent," the above parenthetical is instead describing the *amount* of a component that

is "sufficient" to be "therapeutically active." That amount can either be 1) "a therapeutically effective amount" or 2) "an amount that exerts a desired medically beneficial effect." This does not redefine "therapeutic" or "therapeutically active" as "having a desired medically beneficial effect." Nor does it mean that all "desired medically beneficial effects" are "therapeutic." This language serves only to distinguish levels of therapeutic activity—those that are fully effective from those that are merely beneficial.

This distinction, between amounts that are "therapeutically effective" rather than merely beneficial, is entirely consistent with Merck's construction and the plain and ordinary meaning of the terms as relating to the treatment of disease. For example, the patent contemplates combination treatment that employs both chemotherapeutic or radiosensitizing agents in combination with radioactive therapy. *E.g.*, '402 Patent at 3:67-4:3. The former agents may be included in an *amount* that is medically beneficial but that is too small to be "therapeutically effective." For example, a chemotherapeutic may be included in radioactive implants in an amount sufficient to kill trace cancer cells left by radiation treatment, but that is insufficient to be therapeutically effective on its own. Radiosensitizers, which are mentioned frequently throughout the specification, are another important example. These agents, which sensitize tissue to radiation and boost the efficacy of radiation therapy, are "therapeutic" because they are used in the treatment of disease

(specifically, cancer) in conjunction with radioactive agents. However, a "therapeutically active amount" of a radiosensitizer is not "therapeutically effective" because it cannot *alone* effectively treat a disease. Thus, a therapeutically active ***amount*** of a radiosensitizer is one that has the medically beneficial effect of sensitizing cancerous tissue to radiation, the latter of which is "therapeutically effective" in treating the disease. Therefore, contrary to Microspherix's suggestion, the phrase "desired medically beneficial effect" is not redefining the scope of "therapeutic" or "prophylactic" but is instead describing one level of such activity (*i.e.*, one that has a desired medically beneficial effect in treating or preventing disease). Thus, while Microspherix copies a phrase from the specification into its construction, that phrase has no bearing on the plain and ordinary meaning of "therapeutic agent" or "prophylactic agent."

Conceding that the above language is incomplete, Microspherix's construction also borrows the concepts of "physiological effect" and "physiological condition" from yet another unrelated phrase in the specification. Microspherix again refers to Section IV. ("Method of Making Brachytherapy Strand for Implantation"), which describes Figures 1 and 2 of the invention:

> ***As discussed above***, the therapeutically active component **14** is a material that can be (a) implanted in a target tissue of an animal subject (e.g., a mammal such as a human patient) **to exert an effect on the animal's physiology**, and (b) associated with the biocompatible component **12** in the brachytherapy strand **10.**

'402 Patent at 16:36-41. Once again, the phrase Microspherix relies upon does not purport to define "therapeutic agent" or "prophylactic agent." The sentence instead refers expressly to the above section of the specification, which describes the therapeutic and prophylactic agents of the invention. That a therapeutic or prophylactic agent can "exert an effect on the animal's physiology" does not indicate that *all* agents exerting physiological effects are therefore definitionally "therapeutic" or "prophylactic." Even Microspherix recognizes this, concocting a limitation on the scope of the physiological effects that are "therapeutic" within its constructions to those that are "desired" and "beneficial" (and those that are prevented by "prophylactic" agents to those that are "undesired or non-beneficial"). If the above phrase in the specification *defined* the scope of "therapeutic" as Microspherix implies, rather than simply being *compatible* with it, Microspherix's own construction would be improperly limited via Microspherix's inclusion of the concepts of desired/undesired and beneficial/non-beneficial. Microspherix's constructions thus derive their boundaries from neither the plain and ordinary meaning nor the language of the specification, but instead from Microspherix's need to expand the meaning of the terms for infringement.

Having failed to provide a basis for its own artificial definition of "therapeutic agent" and "prophylactic agent," Microspherix suggests that Merck's construction improperly limits the specification. As discussed above, Section I.C. sets forth the

"Therapeutic and Diagnostic Agents" to be included in the "Brachytherapy Strands" of the invention. The relevant portion begins: "[a]ny of a wide range of therapeutic, diagnostic and prophylactic materials can be incorporated into the strands, including" various broad classes of materials such as "organic compounds" and "inorganic compounds." '402 Patent at 7:65-8:3. This passage relies on the adjectives "therapeutic" and "prophylactic" to define the scope of "materials" that "can be incorporated into the strands." The specification subsequently says that "[t]he non-radioactive drug can take the form of . . . hormones," among more than a dozen other classes of compounds such as "cytostatic, cytotoxic, and cytocidal agents." *Id.* at 8:4-10. As with the preceding sentence discussing the "wide range" of such agents, these enumerated classes fall under the umbrella of "therapeutic, diagnostic and prophylactic," and thus do not *define* those descriptors but instead are *limited* by them. This is entirely consistent with Merck's construction: there are numerous "therapeutic hormones" (*i.e.*, hormones "for the treatment of disease"), including the sole hormone enumerated as an example in the patent, leuprolide, which is used as a "treatment for prostate cancer." *Id.* at 16:51-55.

To support the breadth it needs for infringement, Microspherix seizes on the word "hormones," assumes without any basis that the specification is invoking contraceptive hormones, then reasons backwards to an expansion of the meaning of "therapeutic," suggesting that Merck reads out this fabricated embodiment. MX Op.

Br. at 12. This is circular—it erroneously assumes the very proposition that Microspherix advances, which is that contraceptive hormones are "therapeutic."[9]

In the context of the Asserted Patents, extending Microspherix's logic leads to absurd results. For example, the patent states that the "therapeutic, diagnostic, and prophylactic materials" may take the form of "organic compounds" and "inorganic compounds." '402 Patent at 7:65-8:3. If all "organic" and "inorganic" compounds, which by definition cover all substances known to man, may be included in the invention, rather than only those that are "therapeutic, diagnostic, and prophylactic" and can be employed for localized delivery, the specification would be disclosing the inclusion of anything and everything in its implants, no matter how nonsensical. Nor does Microspherix's construction even purport to include all drugs from within the enumerated classes. "Cytotoxic" agents encompass chemical weapons banned by the Geneva Convention (*e.g.*, sarin), which have no "medically beneficial" effects. It is thus clearly not the class (*e.g.*, "inorganic compounds," "cytotoxic . . . agents," "hormones," etc.) that bounds the agents of the invention, but the terms "therapeutic" and "prophylactic" themselves. And these terms have their plain and ordinary meanings as Merck proposes.

[9] Microspherix's citation (at 12-13) to the IPR petition is of no moment. As Merck noted there (and throughout its invalidity contentions), Merck was adopting Microspherix's apparent interpretation in arguing under the "broadest reasonable interpretation" standard that applied in IPR but does not apply here. *See* '402 Pet. (Ex. 37) at 11 n.2.

Although Microspherix purports to derive its construction from the language of the specification, it is actually seeking to expand the ordinary meaning of the terms (*i.e.*, agents for the treatment/prevention of disease) to accuse Merck's contraceptive agents (which neither treat nor prevent disease) of infringement. Having departed from the ordinary meaning, Microspherix has to fabricate its own boundaries (*e.g.*, "desired"/"undesired" or "medically beneficial"/"non-beneficial") to avoid the above absurd results. The Court should reject Microspherix's proposal.

III. TERMS RELATED TO CONFIGURATION OF THE IMPLANTS

A. "marker component"

Consistent with the use of the term "component" in the specification and claims, the "marker ***component***" is ***the*** part of the seed or strand that ***is a marker***. *See* MRK Op. Br. at 23. Microspherix has neither provided a meaningful construction for "marker component" nor made any arguments in support of its constructions or in opposition to Merck's. MX Op. Br. at 6-8. Microspherix has therefore waived opposition to Merck's construction, and the Court should adopt it.

B. "hollow interior" / "wherein the agent is disposed within the hollow interior of the tube"

As set forth in Merck's opening brief, Merck's construction gives meaning to the term "hollow" and is consistent with both the language of the specification and the commonly understood meaning of the term. In contrast, Microspherix acknowledges that it is improperly eliminating meaning from the term "hollow."

The Court should adopt Merck's construction.

Microspherix argues that the requirement in Merck's construction that "hollow interior" requires an "empty space" conflicts with claim language that places other components in said interior. But Merck's construction is not at all inconsistent with the claim language Microspherix points to. "Hollow interior" describes a physical feature of the "marker component"—*i.e.*, the empty space "bound[e]d" by its "substantially continuous wall." The placement of other components within that empty space does not alter the structure of the marker component. The specification uses the term "hollow" in precisely this manner. Figure 2 depicts "a brachytherapy strand . . . shaped into a hollow tube." The specification indicates that "FIG. 2 can be modified by *filling the cylindrical cavity* 20 [*i.e.*, a hollow cavity] with a hydrogel, including a therapeutically active substance, and capping off the ends of the *hollow tube* 18." '402 Patent at 17:56-59. Thus, despite the cavity's being filled with a polymer and agent, the specification still describes the structure as "hollow."

Microspherix's construction eliminates entirely the meaning of the term "hollow" (*see* MX Op. Br. at 21) in violation of the fundamental claim construction principle that all claim terms be given meaning. *Merck & Co. v. Teva Pharm. USA, Inc.*, 395 F.3d 1364, 1372 (Fed. Cir. 2005). Consistent with the use of "hollow" in the specification, the term carries meaning even when the empty space is

subsequently filled because it defines the structure of another element (*e.g.*, the "tube" in Fig. 2). The inventor could otherwise have used the term "interior" alone.

Microspherix attacks a strawman argument, suggesting that Merck requires the "hollow interior" remain empty "after the agent or other components are disposed within the strand or tube," and characterizing Merck's construction as "an empty space post-disposal." MX Op. Br. at 21-23. But Merck's construction does no such thing; rather, as explained above, it simply defines a structural element of the claimed implants in line with the intrinsic record. "Hollow interior" is the space "bound[ed]" by the "substantially continuous wall" of the "marker component" and thus describes its structure. To the extent other claim limitations require that the "empty space" in the marker component be partially or completely filled with other components, those limitations already provide for the filling of the empty space without adjusting the meaning of "hollow interior." Unnecessarily incorporating these other claim limitations into the definition of "hollow interior" renders the word "hollow" meaningless, and the Court should thus reject Microspherix's construction.

C. "[marker component] . . . having a substantially continuous wall bounding a hollow interior" / "[marker component] . . . having a substantially continuous wall along the length, the substantially continuous wall bounding a hollow interior"

As set forth in Merck's opening brief, Merck's construction is dictated by the plain language of the claims and the specification. Despite having Merck's construction since July 2018, Microspherix has neither proposed an actual

construction for this term nor disputed Merck's construction. In its opening brief, Microspherix simply states that its constructions of "hollow interior" and "marker" suffice to address "the disputed aspects of these terms." Since Microspherix does not dispute Merck's construction that "the marker component itself constitutes a wall that defines the hollow interior," Microspherix has waived any construction of its own, and the Court should enter Merck's construction as undisputed.

D. "polymeric coating"

The parties dispute the plain and ordinary meaning of "polymeric coating." Merck's proposal is supported by the intrinsic and extrinsic record, including expert testimony. The Asserted Patents describe coatings as formed by typical prior art processes in which polymer is applied to or built up on existing surfaces. MRK Op. Br. at 28-29; '402 Patent at 13:36-14:19. The Asserted Patents do not depart from the plain meaning of the term—a POSA would already understand that a "polymeric coating" is a polymer layer that is formed as the result of those very processes. Park Decl. ¶¶ 87-89. Microspherix's construction, on the other hand, finds no support in the intrinsic or extrinsic record, contradicts its other litigation positions, and improperly renders "coating" meaningless.

Microspherix again provides no explanation or evidence for its assertion that its construction represents the "plain and ordinary meaning." Without explanation, Microspherix cites portions of the intrinsic record that actually support Merck's

construction and fail to support Microspherix's expansive proposal. For example, Microspherix, without any explanation, points to the specification's disclosure of the "phase inversion method" for "forming or coating seeds." MX Op. Br. at 18 (citing '402 Patent at 12:32-39). This disclosure *distinguishes* between the polymer being "coated" on the particles from a result where "the particles are dispersed in the polymer." '402 Patent at 12:32-40; *see also* Park Decl. ¶ 48. In other words, the specification draws a distinction between using polymers to ***form*** seeds/strands and using polymers to ***coat*** existing particles. MRK Op. Br. at 29-30. This disclosure thus supports Merck's construction because a coating denotes a distinct process and not just any process that could result in a layer of polymer. Microspherix also confusingly points to the Wurster air-suspension coating process with no explanation as to how this is inconsistent with Merck's construction or supports its own construction. MX Op. Br. at 18-19. As Merck has explained, in this prior art coating process, "a uniform coating is built up on the seeds or strands." MRK Op. Br. at 28-29 (citing '402 Patent at 13:36-14:19). Again, this supports Merck's construction.

Microspherix also points to a preliminary amendment in prosecution in which Microspherix simply directs the Examiner to two portions of the specification as written description support for "polymeric coating." MX Op. Br. at 19 (citing MX Ex. 10 at 2-4.) These portions are precisely those Merck has identified as supporting

its construction and do nothing to help Microspherix. *Compare* MRK Op. Br. at 29, *with* MX Ex. 10 at 2-4 (citing what is now '402 Patent at 7:63-65, 13:37-40).

The crux of Microspherix's opposition to Merck's construction is that it improperly requires a product-by-process limitation. But Microspherix's argument is belied by its own litigation positions. Microspherix has distinguished between a "polymeric coating" and other polymer layers based on the process by which the layer was formed. MRK Op. Br. at 29-30. For example, claims in a related Kaplan patent distinguish between a "coating" and a "sleeve," and Microspherix has argued that prior art "sheaths" and "hulls" cannot be "coatings." '310 Patent (Ex. 14) at Cls. 39-42; MX Val. Cont. (Ex. 15) at 28. Polymer sleeves, sheaths, and hulls are all "layers of polymer" that are distinct from "polymeric coatings" only in the manner in which the polymer layer was formed; the former are formed as separate structures and slid over or filled with other substances, and the latter is formed by applying or building up polymer on an existing surface.

As described in Merck's opening brief, Microspherix's proposal appears to have been fabricated to support its infringement contentions against Merck's Nexplanon product, which has no "coating" at all. MRK Op. Br. at 30-31. In expanding the definition of "polymeric coating" from its ordinary meaning to encompass any "layer of polymer," Microspherix has not only ignored the plain and ordinary meaning to skilled artisans, it has rendered the term "coating" meaningless

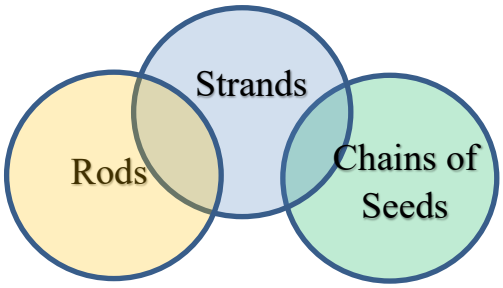
and violated common sense. For example, under Microspherix's construction, if a thin slab of polymer (*e.g.*, a flat polymeric disc) were dip-coated in and thus surrounded by another material, the thin slab would be a "polymeric *coating*" despite forming the *inner core* of the resulting product because it is "a layer of polymer."[10] A POSA would not consider a polymer core to be a "coating." The Court should adopt Merck's construction.

E. "rod"

The parties dispute whether the plain meaning of "rod" encompasses chains or continuous arrays of seeds. As Merck explained in its opening brief, both the intrinsic record and common sense dictate that it does not. MRK Op. Br. at 31-32. Microspherix, on the other hand, contends that a "rod" encompasses a chain of seeds, and to support this conclusion, Microspherix, relying on citations pertaining only to strands and not rods, conflates "strand" and "rod" to argue that "the claimed ***rod*** can comprise more than one single cylinder." MX Op. Br. at 29. Microspherix employs the following flawed logic: because some strands are chains or continuous arrays of seeds, and some strands are rods, therefore, some rods are chains or continuous arrays of seeds (*e.g.*, cylindrical seeds). As the below illustrates, though some

[10] That a subsequent claim limitation in the independent claim of the '402 dictates that the "polymeric coating ***covers*** the strand," and thus could not be in the core of the claimed implants, is of no moment. Microspherix's construction gives no meaning to the term "coating" in violation of basic claim construction principles.

strands may be chains or continuous arrays of seeds, it does not follow that rods (a separate sub-species of strands) can be chains or continuous arrays of seeds.



Microspherix's position is thus baseless. Merck's construction, which is supported by uncontroverted intrinsic and extrinsic evidence including dictionaries (MRK Op. Br. at 32), should be adopted.

F. "flexible"

As explained in Merck's opening brief, to the extent this term requires construction, Merck's proposal reflects the ordinary meaning of flexible that even Microspherix and its expert advanced during the IPRs. MRK Op. Br. at 32-33. Microspherix's attempt to define flexible in terms of *what it is not* contradicts the specification, which does not treat flexible as exclusive of rigid or flaccid.[11] '402 Patent at Abstract, 4:8-11, 22:23-25, 22:32-35. That other courts have declined to construe the term and instead given it its "plain and ordinary meaning" is inapposite in the context of these patents (which were not at issue before those courts) and in

[11] Regarding Microspherix's argument that "capable of bending" somehow excludes flexibility "in any direction," it is unclear what flexibility "in any direction" means, and Microspherix provides no explanation. MX Op. Br. at 25. Nevertheless, Merck would be amenable to the construction "capable of bending in any direction."

this jurisdiction, which requires a construction for plain and ordinary meaning. *See* L. Pat. R. 4.2(a). Moreover, to the extent other courts' handling of "flexible" is relevant, numerous courts have construed "flexible" in line with Merck's construction. *See, e.g.*, *STMicroelectronics, Inc. v. Sandisk Corp.*, 2006 WL 6222492, at *3 (E.D. Tex. June 20, 2006) ("capable of being bent"); *Lydall Thermal/Acoustical, Inc. v. Fed. Mogul Corp.*, 566 F. Supp. 2d 602, 611 (E.D. Mich. 2008), *aff'd*, 344 F. App'x 607 (Fed. Cir. 2009) ("capable of being bent or flexed").

While Merck disagrees with Microspherix's arguments that this term is not indefinite, Merck will present its indefiniteness arguments during the merits phase of the case, as the parties expressly agreed upon in the JCCPS. D.I. 94-1.

IV. CONSTRUCTIONS NECESSITATED BY THE IPR RECORD

A. "marker" / "radiopaque material" / "radio-opaque material" / "agent selected from the group consisting of radiopaque"

As explained in Merck's opening brief, the asserted claims avoided invalidation only because of Microspherix's arguments to the PTAB that a *barium sulfate* marker is too toxic for inclusion in implants with open ends, openings, or pores through which the barium sulfate could escape. MRK Op. Br. at 33-35. Those claims of the Asserted Patents without such openings, and thus without a risk of releasing the supposedly unacceptably toxic barium sulfate, were invalidated. '402 FWD (Ex. 5) at 27. Microspherix's argument that a POSA would not have succeeded in achieving *the claimed invention* when adding barium sulfate to an

implant that otherwise indisputably discloses all claim limitations *presumes* a limitation on the toxicity of the selected marker or radiopaque material. The PTAB expressly acknowledged that such an argument necessitates a corresponding claim limitation, and both accepted and relied upon Microspherix's position that barium sulfate was too toxic. *Id.* at 25-26, n.15, 32-33. Microspherix cannot now erase this part of the intrinsic record to maintain its infringement-driven proposed construction. The Court should enter Merck's construction, which reflects the limitation that Microspherix adopted to salvage its remaining claims.

Microspherix advocated (successfully) for the very claim limitation it now seeks to avoid via its arguments regarding the "reasonable expectation of success" inquiry for obviousness. To prove that a patent is obvious, a patent challenger must demonstrate that all limitations were present in the prior art, and that a POSA would 1) be motivated to combine those elements into the claimed invention and 2) have a reasonable expectation of success in doing so. *PAR Pharm., Inc. v. Twi Pharms., Inc.*, 773 F.3d 1186, 1193 (Fed. Cir. 2014). As the Federal Circuit has explained, the latter inquiry must focus on "a reasonable expectation of achieving ***what is claimed in the patent-at-issue***." *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.,* 821 F.3d 1359, 1367 (Fed. Cir. 2016).

In *Illumina*, the PTAB considered this issue regarding a patent related to methods for the use of nucleotide labels. Specifically at issue were methods of

"protecting" "the natural linking process between nucleotides" so the individual nucleotides could be detected, identified and sequenced. Petitioner argued that the claims were obvious over a patent publication ("Tsien"), which describes "a process for labeling, and ultimately sequencing, a nucleic acid molecule," and an article ("Zavgorodny"), which describes a particular protecting group required by the challenged patent claims. Petitioner argued that a POSA, "to improve the efficiency, reliability, and robustness of the sequencing [] method taught in Tsien," would have used protecting groups that meet the criteria of Tsien, such as the protecting group taught by Zavgorodny. *Id.* at 1364. Patentee argued that a POSA would not have a reasonable expectation that the protecting group of Zavgorodny would succeed in meeting "the specific criteria ***of Tsien***," which requires a specific type of removal, "***quantitative*** removal," of the protecting group.

Critically, the claims at issue in *Illumina* did not recite "quantitative" removal, only requiring that the protecting group can be "modified *or* removed." *Id.* The PTAB improperly accepted patentee's argument and rejected petitioner's obviousness challenge. On appeal, the Federal Circuit held that "because the claims do not require quantitative removal, the Board erred by imposing such a requirement through *the reasonable expectation of success analysis*." *Id.* at 1367. The Federal Circuit explained that "claim 1 does not require . . . quantitative removal," and "[a]ccordingly, it is of ***no moment*** that Zavgorodny's protecting group would not be

removed quantitatively in Tsien['s] sequencing method—removal is ***simply not required by the claim of the [challenged] patent***." *Id.* Patentee's argument could only have been correct if the challenged claims expressly or inherently contained the limitation that there was no expectation of successfully achieving: quantitative removal of the protecting group.

Similarly here, Microspherix argued in IPR that a POSA would lack a reasonable expectation of success in using barium sulfate as a marker because it is too toxic for implants with openings, thereby establishing as a matter of law an inherent claim limitation: that the marker/radiopaque material be less toxic than barium sulfate.[12] The Board agreed with Microspherix that a POSA would lack a reasonable expectation of success in achieving the claimed invention because barium sulfate would be too toxic for inclusion in open implants:

> ***Because*** **barium sulfate was known to be toxic and leaching of the material from devices was a concern to an ordinary artisan at the time the invention was made**, we are not persuaded that Petitioner has shown a person of ordinary skill in the art to have had **a reasonable expectation of successfully** combining De Nijs and Schopflin for purposes of claims 6 and 9.

'402 FWD (Ex. 5) at 32.

[12] The PTAB, agreeing with Merck regarding the Federal Circuit's holding in *Illumina*, rejected an alternative expectation-of-success argument from Microspherix regarding barium sulfate's impact on the "release rate" of the therapeutic agent. Specifically, the Board found that "Patent Owner's arguments relating to the release rate of the therapeutic agent relates to unclaimed subject matter." '402 FWD (Ex. 5) at 25-26 (citing *Illumina*).

If a low-toxicity marker was "simply not required by the claim" as Microspherix now argues, Microspherix's IPR arguments about toxicity would have been "of no moment" to Merck's obviousness challenge. *Illumina*, 821 F.3d at 1367. Thus, Microspherix and the PTAB consciously and deliberately agreed that the claims have a toxicity limitation to the exclusion of barium sulfate.[13] And the Federal Circuit agreed. *Merck Sharp & Dohme Corp. v. Microspherix LLC*, 814 F. App'x 575 (Fed. Cir. 2020). This constitutes clear prosecution history disclaimer.[14] *Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1576 (1995); *Aylus Networks, Inc. v. Apple Inc.*, 856 F.3d 1353, 1360 (Fed. Cir. 2017).

Furthermore, to construe Microspherix's claims as covering barium sulfate would push the patent far beyond what the specification enables. Microspherix and its expert argued during the IPR that the potential toxicity of any barium sulfate released from an open-ended implant, regardless of the quantity of barium sulfate contained within or potentially released from said implant, would prevent a POSA

---

[13] While there was no evidence of record as to an objective threshold for any potential toxicity, the Court need not reach that issue in deciding claim construction. The IPR record makes clear that at least barium sulfate is too toxic. Merck's construction thus fully resolves the parties' dispute.

[14] That Microspherix also successfully argued in IPR that a POSA would lack a motivation to combine barium sulfate with an open-ended device is of no moment to disclaimer. *Saffran v. Johnson & Johnson*, 712 F.3d 549, 559 (Fed. Cir. 2013) ("[A]s we have made clear, an applicant's argument that a prior art reference is distinguishable on a particular ground can serve as a disclaimer of claim scope even if the applicant distinguishes the reference on other grounds as well.").

from expecting to succeed in adding barium sulfate to such an implant. For the Asserted Patents to claim barium sulfate in open implants and thus enable having overcome the alleged deficit in the state of the art as to managing barium sulfate toxicity, the specification would have to provide guidance for doing so. But *as Microspherix agrees in its opening brief*, "the patent never mentions toxicity when listing the various possible marker materials that might be used[.]" MX Op. Br. at 7. Nor does the patent describe the inclusion of a marker in implants with openings or once mention barium sulfate, despite its common use in prior art. *See* '402 PER (Ex. 38) at 8-9. Merck's construction is thus consistent with construing the claims to preserve validity. *Bed Bath & Beyond Inc. v. Sears Brands, LLC*, 2010 WL 4291505, at *9 (D.N.J. Oct. 22, 2010) (construing "retail" terms as limited to physical locations to the exclusion of websites where broader construction "would leave the claim terms with no enabling disclosure").

Despite its successful IPR arguments, Microspherix now argues that the specification simply states that "any substance" can be used as the "marker" if it can be "detected by conventional x-ray imaging techniques." MX Op. Br. at 6-7. Microspherix should be judicially estopped from successfully arguing one thing to the PTAB to save the patents' validity, and arguing the opposite before this Court as a means to sustain its infringement allegations. *New Hampshire v. Maine*, 532 U.S. 742, 750–51 (2001). As discussed in Merck's opening brief, however, a finding of

prosecution history estoppel or judicial estoppel is not required: Microspherix's IPR positions are highly relevant to the claim construction inquiry and clearly dictate that including barium sulfate in open implants is outside the scope of the invention, consistent with the specification's complete lack of guidance for doing so. MRK Op. Br. at 37-38. The Court should hold Microspherix to the positions it took in IPR to save the validity of its claims and enter Merck's construction.

B. "radiopaque" / "radio-opaque"

The parties appear to agree that for something to be "radiopaque," it should ***actually*** appear on x-ray imaging. Microspherix argues that its construction requires a specific level of image clarity, but fails to point to any support for distinguishing between detections (or visualizations) that are "shadows, pixelated images, or cloudy images" and those that are not. MX Op. Br. at 10-11. The intrinsic record is silent as to clarity when imaging radiopaque materials. Merck's construction, which Microspherix previously proposed, is lifted from the specification. '402 Patent at 10:21 ("radiopaque (detectable by x-ray)"), 10:25-26 ("detected by conventional x-ray imaging techniques."). The Court should thus adopt Merck's construction.

Dated: January 14, 2021

Respectfully submitted,

GIBSON, DUNN & CRUTCHER LLP

Tracey B. Davies (*admitted pro hac vice*)
Betty X. Yang (*admitted pro hac vice*)
GIBSON, DUNN & CRUTCHER, LLP
2001 Ross Avenue, Suite 2100
Dallas, TX 75201
Tel: (214) 698-3100
Fax: (214) 571-2900
tdavies@gibsondunn.com
byang@gibsondunn.com

Y. Ernest Hsin (*admitted pro hac vice*)
GIBSON, DUNN & CRUTCHER LLP
555 Mission Street
San Francisco, CA 9410575201
Tel: (415) 393-8200
ehsin@gibsondunn.com

Andrew P. Blythe (*admitted pro hac vice*)
GIBSON, DUNN & CRUTCHER, LLP
333 South Grand Avenue
Los Angeles, CA 90071
(213) 229-7000
ablythe@gibsondunn.com

MCCARTER & ENGLISH, LLP

/s/ John E. Flaherty

John E. Flaherty
Ravin R. Patel
MCCARTER & ENGLISH, LLP
Four Gateway Center
100 Mulberry St.
Newark, New Jersey 07102
(973) 622-4444
jflaherty@mccarter.com
rpatel@mccarter.com

CERTIFICATE OF SERVICE

I hereby certify that on January 14, 2021, I caused a true and correct copy of Defendants' Responsive Claim Construction Brief and supporting documents to filed on the Court's CM/ECF system, which will provide notice and constitutes service on all counsel of record. Copies of all documents filed have been served on counsel for Plaintiff by way of email.

/s/ John E. Flaherty
John E. Flaherty